March 14, 2002

To: All Licensed Health Care Service Plan Medical Directors

From: Antonio Linares, M.D., Medical Advisor
Department of Managed Health Care

RE: Clinical Review of HIV-related Lipodystrophy (Lipoatrophy and Fat Accumulation) and Interpretation of Coverage Under AB 1621 Plan Requirements.

DMHC Findings and the Need for Consensus:

The Department of Managed Health Care (Department) has encountered instances where enrollees were evaluated inconsistently for HIV-wasting and related syndromes (such as lipodystrophy) by providers using different standards. Additionally, some treatments for these conditions were initially denied on the basis that the treatment was cosmetic rather than medical or considered to be experimental. Based on these findings, a clinical update was requested to promote a greater understanding of HIV-wasting related syndromes and the application of AB 1621 for reconstructive surgery procedures.

The Department recognizes that the medical community has not yet established consistent standards for evaluating and treating some of these conditions. Although there are no established guidelines for the treatment of HIV-related lipodystrophy, it is recognized by the Department that treatment for the clinical complications resulting in abnormal body structure appearance may include reconstructive surgery coverage under AB 1621.

In approaching complaints and requests for Independent Medical Review related to treatments for HIV-wasting, lipodystrophy and related metabolic or nutritional complications, the Department will consider the following clinical summary. This information will be used in the evaluation of such claims and the application of AB 1621. It is important to note and acknowledge that health plan medical directors and HIV-medicine experts provided input into the research and review of this clinical summary.

Background of Current Clinical Issues:

HIV-infection and/or complications related to treatment with protease inhibitors (PI) or highly active anti-retroviral therapy (HAART) may result in nutritional, metabolic or body composition disorders. The incidence of protein-energy malnutrition (wasting syndrome) in HIV-infected patients has decreased since 1996. Clinically, the most important consideration is that HIV-wasting is more likely to occur in the setting of a secondary infection, diarrhea, anorexia, mal-absorption and with immunological or virological failure.

The FDA reported in June 1997 increasing adverse events related to abnormal distribution of body fat (lipodystrophy) in patients receiving PI therapy. The major issue clinically, is distinguishing between HIV-wasting of protein-energy malnutrition and that of the lipoatrophy (fat wasting) associated with the lipodystrophy syndrome. This distinction can be difficult to make yet it is critical so that appropriate treatment can be applied.[1]

The mechanism leading to HIV-wasting or the etiology of fat mal-distribution among HIV-infected patients is unknown. In the medical literature there is no universally accepted definition of HIV-related lipodystrophy or related wasting syndrome.[2] There is also limited data related to the treatment of choice for lipodystrophy. Kevin Frost, the Vice President for Clinical Research and Prevention at the American Foundation for AIDS Research, has outlined some of the treatment challenges for care providers in a recent editorial in **The AIDS Reader**[3]. He points to Dr. Abrams work at UC San Francisco where potential treatment regimens for wasting and lipodystrophy must consider the specific needs of individual patients.

Clinical Considerations in the Diagnosis of HIV-Related Syndromes:

1. HIV-wasting or protein-energy malnutrition. Most cases will be characterized by one of the following clinical findings:
    - loss of skeletal muscle mass
    - general cachexia
    - vitamin and mineral deficiency

    Loss of skeletal muscle mass can be difficult to determine clinically. A person's weight may remain unchanged but have a loss of muscle mass. The CDC defines HIV-wasting as a 10% loss of weight from baseline in the presence of diarrhea or weakness for 30 days. The CDC does not address muscle mass or nutritional status in the definition.[4]

    HIV-related lipodystrophy: Most cases will be characterized by body fat composition changes related to abnormal distribution (fat depletion, accumulation

[1] Correspondence from Michael Reyes, MD, Cristina Gruta, Pharm D and Jason Tokumoto, MD, et al.
[2] HIV/AIDS Clinical Management Volume 3, Optimizing Antiretroviral Therapy: Strategies and Regimens
[3] The AIDS Reader 11(3): 130-131, 2001, Use of Steroids for Wasting and Lipodystrophy Syndromes in HIV/AIDS
[4] Ibid., fn 1

and/or increased deposition in the viscera). Clinical findings may progress over a two-year period and may include:

- Facial wasting or lipoatrophy (may appear early in lipodystrophy).
- Loss of fat from upper and lower extremities and buttocks.
- Accumulation of fat in subcutaneous tissues of the lower trunk, abdomen, and upper back/neck area (buffalo hump).
- Increased abdominal girth due to increased visceral adipose tissue relative to subcutaneous adipose tissue ratio.
- Fat accumulation in breasts in men and women may also result in pain.

Scevola et al.[5] have published diagnostic criteria for HIV-related lipodystrophy, which is defined by main criteria (total of 4), minor criteria (total of 8), and adjunctive criteria (total of 6).

2. Metabolic, hormonal or nutritional alterations that may be seen with HIV-wasting or lipodystrophy. Clinical findings may include the following:
    - Lipid abnormalities of subnormal HDL, increased triglycerides, increased total cholesterol, increased LDL and a higher risk of atherosclerosis or coronary heart disease.
    - Glucose metabolism disorders including insulin resistance, impaired glucose tolerance, and diabetes mellitus.
    - Bone disorders include osteopenia, osteoporosis, and avascular necrosis.

Clinical Management of Lipodystrophy (Lipoatrophy or Fat Accumulation):

The American Academy of HIV-Medicine has published a monograph series that outlines some of the challenges in understanding the etiology of lipodystrophy and identifying effective treatments.[6] The effectiveness and limitations of growth hormone and exercise to reduce fat accumulation are discussed. The role of PI therapy is also reviewed.

When HIV-related lipoatrophy (fat loss) is diagnosed and is complicated by the clinical findings of abnormal body structure appearance, coverage for reconstructive surgery may apply under AB 1621. The Health and Safety Code §1367.63 requires that the surgery performed must improve function or create a normal appearance in accordance with the standard of care as practiced by physicians specializing in reconstructive surgery. Upon recommendation of a plan reconstructive surgeon, treatments like silicone type injections to correct or repair abnormal body structures due to lipoatrophy are covered under AB 1621 if the treatment offers more than a minimal improvement in appearance.

In conclusion, this Medical Advisory report was requested to address concerns related to the lack of consensus and/or consistent definitions for HIV-related wasting syndromes. This report will be discussed at the next Clinical Advisory Panel meeting on

[5] Scevola et al., The AIDS Reader, June 2000:365-375

[6] AAHIVM, Clinical Data on The Recent Educational Objectives of The AAHIVM 2001 Core Curriculum, AAHIVM Monograph No. 1 Los Angeles: American Academy of HIV Medicine, December 2001

March 20th, 2002. Any questions you may have should be forwarded to my office via Phillis Soresi at (psoresi@dmhc.ca.gov) prior to that meeting.